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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/875,076	06/06/2001	Chen W. Liaw	AREN-011DIV (11.US9.DIV)	6379

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EXAMINER	
LOCKARD, JON MCCLELLAND	
ART UNIT	PAPER NUMBER
1647	

MAIL DATE	DELIVERY MODE
05/28/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/875,076	LIAW ET AL.	
	Examiner	Art Unit	
	JON M. LOCKARD	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 March 2008*.

2a)☒ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *77-101,107 and 108* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *77-101,107 and 108* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03 March 2008* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/4/08, 3/28/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments, and/or Claims

1. The amendment of 03 March 2008 has been entered in full. Claims 107 and 108 have been added. Therefore, claims 77-101 and 107-108 are pending and the subject of this Office action.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Withdrawn Objections and/or Rejections

3. The objection to the Drawings as set forth at pg 3 of the previous Office action (mailed 04 September 2007) is withdrawn in view of Applicants amendment to Figures 3 and 5 (filed 03 March 2008).

Maintained and/or New Objections and/or Rejections

Claim Objections

4. Claim 108 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. In the instant case, the recitation of "wherein the polynucleotide is capable of discriminating between…" in the claim does not further limit the subject matter of the claim from which it depends.

Claim Rejections - 35 USC § 101 and 35 USC § 112, 1st Paragraph

5. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.
>
> The following is a quotation of the first paragraph of 35 U.S.C. 112:
> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 77-101 remain rejected and newly added claims 107-108 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility, or a well established utility. Novel biological molecules lack an established utility and must undergo extensive experimentation to determine an appropriate specific and substantial utility. The basis for this rejection is set forth at pg 4-14 of the previous Office action (mailed 04 September 2007), pg 3-6 of the previous Office Action (mailed 21 March 2003), pg 2-8 of the previous Office Action (mailed 18 March 2005), pg 2-8 of the previous Office Action (mailed 13 October 2005), pg 2-10 of the previous Office Action (mailed 19 May 2006), and pg 2-6 of the previous Office Action (mailed 26 December 2006).

7. The instant application discloses an isolated hARE-2 polypeptide with an amino acid sequence set forth as SEQ ID NO:20 that is encoded by the claimed polynucleotide of SEQ ID NO:19. The specification asserts that the hARE-2 polypeptide encoded by the claimed polynucleotide of the instant invention is believed to be a G-protein coupled receptor (GPCR),

having 53% homology with the orphan GPCR GPR27 (See Table A, pg 8). The Specification discloses that hARE-2 is expressed in the left and right cerebellum and the substantia nigra (See Table C, pg 27). The specification also teaches that the disclosed human orphan GPCRs may be used for the direct identification of candidate compounds as inverse agonists, agonists, or partial agonists for use as pharmaceutical agents (See pg 15, lines 14-16). There is no well-established utility for a specific hARE-2 nucleic acid or amino acid sequence, and the specification fails to disclose a specific and substantial utility for the claimed invention. The instant application does not disclose a specific biological role for the claimed hARE-2 nucleic acid or the protein encoded by it, or its significance to a particular disease, disorder, or physiological process which one would manipulate for a desired physiological or clinical effect. The rejection of the claims under 35 USC § 101 and 35 USC § 112, 1st Paragraph is maintained for reasons of record in the Office actions listed *supra*, only new arguments will be addressed herein.

8. Applicant's arguments (filed 19 June 2007) as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

9. Applicant argues at pg 7 of the response (filed 03 March 2008) that any gene that is selectively expressed in the substantia nigra is useful as a probe for the analysis of cell degeneration of the substantia nigra, whether or not the gene is specifically expressed in dopaminergic cells. Applicant argues at pg 8 of the response that since it is known that the substantia nigra undergoes extensive degeneration during Parkinson's disease, as such the claimed polynucleotides my be used in a number of applications, including (a) the analysis of a

brain for disease-related changes in the architecture of the substantia nigra; (b) to evaluate generalized cell damage versus cell type-specific damage in the substantia nigra; and (c) as a marker for counting cells in the substantia nigra in order to provide an evaluation of disease severity. Applicant argues at pg 9 of the response that the claimed polynucleotide can also be employed to discriminate between a human tissue selected from the right cerebellum, left cerebellum, or substantia nigra and an other human tissue.

10. Applicant's arguments (filed 03 March 2008) have been fully considered but are not persuasive for the following reasons. These asserted utilities are not specific as they can be applied to any polynucleotide that is expressed in the substantia nigra. According to MPEP 2107.01(I)(A),

> "[A] specific utility is specific to the subject matter claimed and can "provide a well-defined and particular benefit to the public." In re Fisher, 421 F.3d 1365, 1371, 76 USPQ2d 1225, 1230 (Fed. Cir. 2005). This contrasts with a general utility that would be applicable to the broad class of the invention."

In the instant case, these asserted utilities do not rely upon any specific structural or functional property of the claimed polynucleotides, but are applicable to the broad class of the invention. Thus, since any polynucleotide that is expressed in the substantia nigra could be used for these asserted utilities, they are not specific to the claimed subject matter. Likewise, the argument that the claimed polynucleotide can also be employed to discriminate between a human tissue selected from the right cerebellum, left cerebellum, or substantia nigra and an other human tissue is also not a specific utility, since any polynucleotide that is expressed in the cerebellum or substantia nigra could be used for this utility.

11. Applicant argues at pg 8 of the response that provided with the knowledge that hARE-2 is expressed selectively in the substantia nigra, a person of ordinary skill in the art would readily appreciate that the claimed polynucleotide is useful for monitoring the production of substantia nigra cells in *in vitro* development systems (e.g. systems for generating substantia nigra cells from neural stem cells), and that stem cell-based treatments for the treatment of Parkinson's disease have long been of interest in the medical community.

12. Applicant's arguments (filed 03 March 2008) have been fully considered but are not persuasive for the following reasons. It is first noted that, contrary to Applicant's assertion, the claimed hARE-2 polynucleotide is not selectively expressed in the substantia nigra, but is also expressed in the cerebellum as well (See Table C, pg 27 of the specification). Thus, the skilled artisan would not readily appreciate that the claimed polynucleotide is useful for monitoring the production of substantia nigra cells since they would not be able to distinguish between the production of substantia nigra cells and cerebellum cells. Moreover, the specification only discloses that claimed hARE-2 polynucleotide is expressed in the substantia nigra, it does not disclose that hARE-2 is expressed in the same population of cells that die in Parkinson's disease. For example, it is well known in the art that the substantia nigra is composed of a heterogeneous population of neurons, the majority of which are either use GABA as their neurotransmitter (i.e., GABAergic) or use dopamine as their neurotransmitter (i.e., dopaminergic) (See for example Hirsch et al., J. Neural Transm. Suppl. 50:79-88, 1997; cited by Applicant 11/17/06). It is also well established in the art that "the generally accepted pathological basis of Parkinson's disease (PD) is the extensive loss of dopaminergic neurons in the zona compacta of the substantia nigra" (See Leenders et al. Arch. Neurol. 47:1290-1298; cited by Applicant 6/19/07). However, the

specification does not disclose that hARE-2 polynucleotide is expressed in the same population of cells that dies in Parkinson's disease, nor has Applicant has not provided any evidence or reference of record to demonstrate that the claimed hARE-2 polynucleotides are expressed in the same cells that die in Parkinson's disease. Therefore, since the specification does not disclose that hARE-2 is expressed in the same population of cells (i.e., dopaminergic neurons) that die in Parkinson's disease, Applicant's assertion that hARE-2 can be employed for monitoring the production of substantia nigra cells for the treatment of Parkinson's disease is not substantial.

13. The Examiner has fully considered all evidence of record and has responded to each substantive element of Applicant's response.

Claim Rejections - 35 USC § 112, 1st Paragraph

14. Claims 77-101 also remain and newly added claims 107-108 are rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. The basis for this rejection is set forth at pg 14 of the previous Office action (mailed 04 September 2007), pg 6 of the previous Office Action (mailed 21 March 2003), pg 8 of the previous Office Action (mailed 18 March 2005), pg 8-9 of the previous Office Action (mailed 13 October 2005), pg 10 of the previous Office Action (mailed 19 May 2006), and pg 6 of the previous Office Action (mailed 26 December 2006).

Summary

15. No claim is allowed.

16. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jon M. Lockard, Ph.D.** whose telephone number is **(571) 272-2717**. The examiner can normally be reached on Monday through Friday, 8:00 AM to 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Manjunath N. Rao, Ph.D.**, can be reached on **(571) 272-0939**. The fax number for the organization where this application or proceeding is assigned is **571-273-8300**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/J. M. L./
Jon M. Lockard, Ph.D.
Examiner, Art Unit 1647
May 24, 2008

/Christine J Saoud/
Primary Examiner, Art Unit 1647